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DATE: Wednesday, May 26, 2004

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| <input type="checkbox"/> | L2 | L1 and (helicobacter or pylori or pylroi or pyloris or pyloridis or hpylori) hpylori) | 36 |
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END OF SEARCH HISTORY

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- ☐ 1. [20040072239](#). 24 Sep 03. 15 Apr 04. Method for controlling the microbiological quality of an aqueous medium and kit therefor. Renaud, Patricia, et al. 435/7.1; G01N033/53.
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- ☐ 3. [20040010012](#). 20 Nov 02. 15 Jan 04. Indole derivatives for the treatment of osteoporosis. Farina, Carlo, et al. 514/323; 514/414 514/419 546/201 548/465 548/494 A61K031/454 A61K031/405 C07D43/02 C07D209/02.
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| Terms | Documents |
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| L1 and (helicobacter or pylori or pylroi or pyloris or pyloridis or hpylori) | 36 |

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L2: Entry 1 of 36

File: PGPB

Apr 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040072239

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040072239 A1

TITLE: Method for controlling the microbiological quality of an aqueous medium and kit therefor

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|------------------------|----------------------------|-------|---------|---------|
| Renaud, Patricia | Le Pecq | | FR | |
| Guillot, Emmanuelle | Saint Germain En Laye | | FR | |
| Mabilat, Claude | Saint Germain Au Mont D'or | | FR | |
| Vachon, Carole | Villeurbanne | | FR | |
| Lacroix, Bruno | Saint Genis Laval | | FR | |
| Vernet, <u>Guy</u> | Albigny Sur Saone | | FR | |
| Charvieu, Marie-Astrid | Charvagneux | | FR | |
| Laffaire, Philippe | Tignieu Jamezieu | | FR | |

APPL-NO: 10/ 332123 [PALM]

DATE FILED: September 24, 2003

FOREIGN-APPL-PRIORITY-DATA:

| COUNTRY | APPL-NO | DOC-ID | APPL-DATE |
|---------|----------|-----------------|--------------|
| FR | 00/08839 | 2000FR-00/08839 | July 6, 2000 |

PCT-DATA:

| DATE-FILED | APPL-NO | PUB-NO | PUB-DATE | 371-DATE | 102 (E) -DATE |
|-------------|----------------|--------|----------|----------|---------------|
| Jul 6, 2001 | PCT/FR01/02191 | | | | |

INT-CL: [07] G01 N 33/53

US-CL-PUBLISHED: 435/007.1

US-CL-CURRENT: 435/7.1

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The invention concerns a method for controlling the microbiological quality of an environmental aqueous medium, suspected of containing various micro-organisms, comprising the following steps: selecting a reference set, consisting of at least three micro-organisms, representing jointly or separately, a microbiological quality level; providing a microbiological detection kit, consisting of at least

three probes specifically and respectively identifying said three micro-organisms; after treating the medium to be analysed, contacting said micro-organisms, or any fraction thereof derived from the medium to be analysed therefrom, with said detection kit, whereby a multiple determination of said micro-organisms is carried out, said determination representing the microbiological quality level of the medium. The invention also concerns an appropriate microbiological detection kit for implementing said method.

First Hit

L3: Entry 2 of 10

File: PGPB

Feb 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040033240

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040033240 A1

TITLE: Immunological combinations for prophylaxis and therapy of helicobacter pylori pylori infection

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY | RULE-47 |
|-------------------|------------|-------|---------|---------|
| <u>Guy, Bruno</u> | Lyon | | FR | |
| Haensler, Jean | Pollionnay | | FR | |

US-CL-CURRENT: 424/234.1

CLAIMS:

1. A composition comprising at least a first and second immunogenic Helicobacter components in a combined amount effective to generate a protective anti-Helicobacter immune response upon administration to an animal at risk of a Helicobacter infection, wherein said at least first and second immunogenic Helicobacter components are independently selected from the group consisting of: a) the Helicobacter AlpA protein or a peptide from said Helicobacter AlpA protein, or a nucleic acid that encodes said Helicobacter AlpA protein or peptide; b) the Helicobacter catalase protein or a peptide from said Helicobacter catalase protein, or a nucleic acid that encodes said Helicobacter catalase protein or peptide; c) the Helicobacter 76K protein or a peptide from said Helicobacter 76K protein, or a nucleic acid that encodes said Helicobacter 76K protein or peptide; d) the Helicobacter 525 protease or a peptide from said Helicobacter 525 protease, or a nucleic acid that encodes said Helicobacter 525 protease or peptide; and e) the Helicobacter urease or a peptide from said Helicobacter urease, or a nucleic acid that encodes said Helicobacter urease or peptide; provided that said first and second immunogenic Helicobacter components are different from each other.

2. The composition according to claim 1, further comprising a third immunogenic Helicobacter component which is independently selected from the group consisting of (a), (b), (c), (d) and (e) as defined in claim 1; provided that said third immunogenic Helicobacter component is different from said first and second immunogenic Helicobacter components.

3. The composition according to claim 2, further comprising a fourth immunogenic Helicobacter component which is independently selected from the group consisting of (a), (b), (c), (d) and (e) as defined in claim 1; provided that said fourth immunogenic Helicobacter component is different from said first, second and third immunogenic Helicobacter components.

4. The composition according to claim 3, further comprising a fifth immunogenic

Helicobacter component which is independently selected from the group consisting of (a), (b), (c), (d) and (e) as defined in claim 1; provided that said fifth immunogenic Helicobacter component is different from said first, second, third and fourth immunogenic Helicobacter components.

5. The composition according to any one of claims 1 to 4, wherein the 76K protein is BabB.

6. The composition according to any one of claims 1 to 5, further comprising an adjuvant.

7. The composition according to claim 6, wherein the adjuvant is a balanced Th1/Th2 adjuvant.

8. The composition according to claim 7, wherein the adjuvant is DC-Chol.

9. A composition comprising, in a combined amount effective to generate a significant therapeutic anti-Helicobacter immune response upon administration to an animal having a Helicobacter infection: (a) the Helicobacter 76K protein or a peptide from said Helicobacter 76K protein; or a nucleic acid that encodes said Helicobacter 76K protein or peptide; or an antibody, or antigen binding fragment thereof that binds to said Helicobacter 76K protein or peptide; (b) the Helicobacter catalase or a peptide from said Helicobacter catalase; or a nucleic acid that encodes said Helicobacter catalase or peptide; or an antibody, or antigen binding fragment thereof that binds to said Helicobacter catalase or peptide; and (c) the Helicobacter 525 protease or a peptide from said Helicobacter 525 protease; or a nucleic acid that encodes said Helicobacter 525 protease or peptide; or an antibody, or antigen binding fragment thereof, that binds to said Helicobacter 525 protease or peptide.

10. The composition according to claim 9, further comprising a fourth immunogenic Helicobacter component which is selected from the group consisting of: (a) the Helicobacter urease or a peptide from said Helicobacter urease; or a nucleic acid that encodes said Helicobacter urease or peptide; or an antibody, or antigen binding fragment thereof that binds to said Helicobacter urease or peptide; and (b) the Helicobacter AlpA protein or a peptide from said Helicobacter AlpA protein; or a nucleic acid that encodes said Helicobacter AlpA protein or peptide; or an antibody, or antigen binding fragment thereof, that binds to said Helicobacter AlpA protein or peptide.

11. A composition comprising at least a first and second immunogenic Helicobacter component in a combined amount effective to generate a significant therapeutic anti-Helicobacter immune response upon administration to an animal having a Helicobacter infection, wherein: (a) said at least first immunogenic Helicobacter component is the Helicobacter AlpA protein or a peptide from said Helicobacter AlpA protein; or a nucleic acid that encodes said Helicobacter AlpA protein or peptide; or an antibody, or antigen binding fragment thereof, that binds to said Helicobacter AlpA protein or peptide; and (b) said at least second immunogenic Helicobacter component is (i) the Helicobacter 76K protein or a peptide from said Helicobacter 76K protein; or a nucleic acid that encodes said Helicobacter 76K protein or peptide; or an antibody, or antigen binding fragment thereof, that binds to said Helicobacter 76K protein or peptide or (ii) Helicobacter catalase or a peptide from said Helicobacter catalase; or a nucleic acid that encodes said Helicobacter catalase or peptide; or an antibody, or antigen binding fragment thereof that binds to said Helicobacter catalase or peptide.

12. The composition according to any one of claims 9 to 11, wherein the 76K protein is BabB.

13. The composition according to any one of claims 9 to 12, further comprising an adjuvant.
14. The composition according to claim 13, wherein the adjuvant is a balanced Th1/Th2 adjuvant.
15. The composition according to claim 14, wherein the adjuvant is DC-Chol.
16. A vaccine comprising the composition according to any one of claims 1 to 15, in a pharmaceutically acceptable excipient.
17. The use of a composition according to any one of claims 1 to 8, in the preparation of a vaccine for protecting an animal against Helicobacter infection.
18. The use of a composition according to any one of claims 9 to 15, in the preparation of a vaccine for treating Helicobacter infection in an animal.

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L3: Entry 7 of 10

File: USPT

Oct 3, 2000

DOCUMENT-IDENTIFIER: US 6126938 A

TITLE: Methods for inducing a mucosal immune response

INVENTOR (1):

Guy; Bruno

Brief Summary Text (15):

Recently, Czinn et al., Vaccine (1993) 11 : 637 have proposed in outline a method of vaccination against Helicobacter pylori, the pathogenic agent of a large number of stomach ulcers. Germ-free mice received a sonicate of H. felis with cholera toxin as adjuvant, via the intragastric route (sonicate administered directly by intubation into the stomach). After a challenge with H. felis, the immunized mice are found to have been protected.

Brief Summary Text (63):

According to a preferred embodiment, the antigen of a bacterium which is pathogenic for the host mammal is an H. pylori antigen, for example the apoenzyme form of H. pylori urease or one of the subunits ureA or ureB of this same urease.

Brief Summary Text (64):

More generally from the standpoint of the method of immunization, and at the same time more precisely targeted from the standpoint of the antigen, it may be pointed out that the subject of the invention is also the use of a DNA fragment coding for an H. pylori antigen in the manufacture of a composition for preventing or treating an H. pylori infection, and for nasal or nasobuccal administration. To this end, the the DNA fragment used as vaccination agent meets the criteria stated above.

Brief Summary Text (68):

Such a composition, when it comprises an antigen of a pathogenic organism which infects the gastric or intestinal mucosa, is useful, in particular, in that it protects the host mammal against the infection in question, in particular affording long-lasting protection, bringing into play memory T and B lymphocytes. Possible infections are those caused by H. pylori, V. cholerae, Shigella flexneri, Shigella sonnei, Salmonella enteritidis, Clostridium difficile, Yersinia enterocolitica, and enterotoxigenic and enteropathogenic E. coli. As regards the antigen, the latter can be the pathogenic agent itself in killed, lysed or attenuated form, or alternatively antigenic components of this pathogen, such as a capsular polysaccharide, or membrane antigens in purified form, or a polypeptide characteristic of this pathogen, either directly purified from the pathogen or obtained by recombinant DNA techniques.

Brief Summary Text (69):

For example, in the case of a composition for preventing H. pylori infections, an antigen of choice may be the apoenzyme of the urease, composed of the subunits A and B, for which the corresponding DNA fragments are described in, e.g., Labigne et al., J. Bact. (1991) 173 (6) : 1920, or one of the subunits of the apoenzyme, or the cytotoxin (WO93/18150), or alternatively proteins of the adhesin family (proteins capable of binding to the receptors of the host cells and which become capable of mediating a coupling of the pathogen to the host cells and of initiating

Drawing Description Text (6):

Drawing Description Text (11):

Detailed Description Text (44):

Detailed Description Text (45):

Detailed Description Text (49):

Detailed Description Text (51):

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encapsulation of the urease, measured by protein assay using the Micro BCA kit (Pierce) is 14.5%. If necessary, the liposome suspension is concentrated by ultrafiltration in a Novacell cell (Filtron) possessing an exclusion limit of 10 kD. kD.

Detailed Description Text (53):

When liposomes are prepared, MPLA (extracted from *E. coli*, Sigma) may be added to the lipid mixture, in the proportion of 1, 2 or 5% relative to the mass of lipid.

Detailed Description Text (68):

Vaccination kit for *H. pylori* infections

Detailed Description Text (69):

Three preparations containing the apoenzyme of *H. pylori* urease, each formulated in a different way depending on the method of administration envisaged, are brought together in a kit.

Detailed Description Text (106):

The apoenzyme form of *H. pylori* urease is encapsulated in liposomes. These liposomes liposomes have an average diameter of 100 nm and a protein content of 60 .mu.g/mg of lipid.

Detailed Description Text (114):

Vaccination kits for *H. pylori* infections (DNA coding for the urease subunit ureB, used as vaccinating agent)

Detailed Description Text (140):

On days 14, 35 and 56, serum samples are drawn from each of the mice. The production of anti-urease antibodies is tested for by ELISA (a purified soluble extract of *H. pylori* is used).

Detailed Description Text (143):

Induction of a mucosal immune response against *H. pylori* urease

Detailed Description Text (145):

0.8 g of DC-Chol and 2.4 g of dioleoylphosphatidylcholine (DOPC) are added to 20 ml of chloroform in a 1 liter round-bottomed flask. This mixture is evaporated under vacuum so as to form a lipid film on the walls of the flask. This film is then dried under a high vacuum overnight.

Detailed Description Text (156):

15 days after the last administration, the mice are challenged by intragastric gavage with 10^{sup.8} microbes of an *H. pylori* strain adapted to mice. One month after challenge, the stomachs are removed and a test of urease activity (Jatrox ND) is performed on 1/4 of the stomach. 4 hours after removal, the optical density of the medium is measured at 550 nm. The results are presented in FIG. 10.

CLAIMS:

7. A method according to claim 6, wherein the antigen is *Helicobacter pylori* antigen.

8. A method according to claim 7, wherein the antigen is the apoenzyme form of *H. pylori* urease.

10. A method according to claim 9, wherein the antigen is *Helicobacter pylori* antigen.

11. A method according to claim 10, wherein the antigen is the apoenzyme form of *H. pylori* urease.

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L3: Entry 7 of 10

File: USPT

Oct 3, 2000

US-PAT-NO: 6126938

DOCUMENT-IDENTIFIER: US 6126938 A

TITLE: Methods for inducing a mucosal immune response

DATE-ISSUED: October 3, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|----------------------------|--------------------------|-------|----------|---------|
| Guy; Bruno | Lyons | | | FR |
| Haensler; Jean | Saint-Genis-les-Ollieres | | | FR |
| Quentin-Millet; Marie-Jose | Villeurbanne | | | FR |

US-CL-CURRENT: [424/184.1](#); [424/199.1](#), [424/234.1](#), [424/278.1](#), [424/282.1](#), [424/812](#),
[514/44](#)

CLAIMS:

What is claimed is:

1. A method for inducing in a mammal, an immune response against an antigen of a pathogen of the respiratory, gastrointestinal, or genitourinary tract at mucosal effector site, which comprises administering a second and a third inducing agent, to said mammal;

wherein said second and third inducing agents are selected independently from the group consisting of the antigen and, provided the antigen is a protein, an expression cassette capable of expressing the antigen in said mammal;

wherein said second inducing agent is administered concomitantly with or prior to the third inducing agent;

wherein said second inducing agent is administered by the nasal or buccal route so that the second inducing agent is targeted to the inducer site(s) for an immune response in the naso-oropharynx or the salivary glands; and

wherein said third inducing agent is administered by a mucosal route other than the nasal route so that the antigen is targeted to the inducer site(s) for the immune response at the effector site at which the immune response is sought.

2. A method according to claim 1, wherein the antigen is a protein.

3. A method according to claim 2, wherein said inducing agent is selected from the group consisting of the antigen and an expression cassette comprising DNA encoding the antigen.

4. A method according to claim 1, wherein the third product is formulated for pulmonary administration.
5. A method according to claim 1, wherein the third product is formulated for urogenital administration.
6. A method according to claim 1, wherein the third product is formulated for oral administration.
7. A method according to claim 6, wherein the antigen is Helicobacter pylori antigen.
8. A method according to claim 7, wherein the antigen is the apoenzyme form of H. pylori urease.
9. A method according to claim 1, wherein the third product is formulated for intragastric administration.
10. A method according to claim 9, wherein the antigen is Helicobacter pylori antigen.
11. A method according to claim 10, wherein the antigen is the apoenzyme form of H. pylori urease.
12. A method according to claim 1, wherein the first product further comprises an adjuvant selected from the group consisting of aluminum hydroxide, aluminum phosphate, and ISCOMs.
13. A method according to claim 1, wherein the second product comprises particles selected from the group consisting of liposomes and microspheres.
14. A method according to claim 13, wherein the particles are from about 0.05 μm to about 5 μm in diameter.
15. A method according to claim 1, wherein the third product comprises particles selected from the group consisting of liposomes and microspheres, and further wherein said third product is formulated for pulmonary, oral, or intragastric administration.
16. A method according to claim 15, wherein the third product comprises particles from about 0.05 to about 5 μm in diameter, and is formulated for pulmonary administration.
17. A method according to claim 16, wherein the second or third product is a spray or an aerosol.
18. A method according to claim 15, wherein the third product comprises particles from about 0.05 to about 5 μm in diameter, and is formulated for oral or intragastric administration.
19. A method according to claim 1, wherein the third product is an enterically protected preparation.
20. A method according to claim 1, wherein the second or third product further comprises a non-toxic adjuvant, other than the non-toxic subunits or the detoxified forms of bacterial toxins and other than liposomes or microspheres.

- 21. A method according to claim 1, wherein the second or third product further comprises the major lipopolysaccharide antigen of a bacteria.
- 22. A method according to claim 1, wherein the inducing agent contained in the first, the second or the third product is the antigen.
- 23. A method according to claim 1, wherein the inducing agents contained in the second and third products are the same.
- 24. A method according to claim 1, wherein the inducing agents contained in the first, second and third products are the same.
- 25. A method according to claim 1, wherein the antigen is pathogenic for the mammal.
- 26. A method according to claim 11, which comprises administering a first inducing agent to said mammal by the systemic route; said first inducing agent being selected from the group consisting of the antigen and, provided the antigen is a protein, an expression cassette capable of expressing the antigen in a mammal.
- 27. A method according to claim 2, wherein the first product is formulated for parenteral administration.
- 28. A method according to claim 27, wherein the first product is formulated for subcutaneous, intradermal or intramuscular administration.

First Hit

End of Result Set

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L3: Entry 10 of 10

File: DWPI

Jul 18, 2002

DERWENT-ACC-NO: 1999-009388

DERWENT-WEEK: 200258

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TITLE: Helicobacter-derived immunogen for use as vaccine - containing extract of Quillaja saponaria, cationic lipid and/or glyco-lipo-peptide as adjuvant

INVENTOR: GUY, B; HAENSLER, J

PRIORITY-DATA: 1997FR-0015732 (December 8, 1997), 1997FR-0005608 (April 30, 1997)

PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|--|-------------------|----------|-------|-------------|
| <input type="checkbox"/> AU 750379 B | July 18, 2002 | | 000 | A61K039/106 |
| <input type="checkbox"/> WO 9848836 A1 | November 5, 1998 | F | 055 | A61K039/106 |
| <input type="checkbox"/> FR 2762787 A1 | November 6, 1998 | | 000 | A61K039/39 |
| <input type="checkbox"/> AU 9876584 A | November 24, 1998 | | 000 | A61K039/106 |
| <input type="checkbox"/> EP 979100 A1 | February 16, 2000 | F | 000 | A61K039/106 |
| <input type="checkbox"/> BR 9809381 A | July 4, 2000 | | 000 | A61K039/106 |
| <input type="checkbox"/> KR 2001020418 A | March 15, 2001 | | 000 | A61K039/106 |
| <input type="checkbox"/> JP 2002505665 W | February 19, 2002 | | 056 | A61K039/106 |

INT-CL (IPC): A61 K 39/02; A61 K 39/106; A61 K 39/39; A61 K 45/00; A61 K 47/00; A61 P 31/04; A61 K 39/02; A61 K 47:26; A61 K 47:42

ABSTRACTED-PUB-NO: WO 9848836A

BASIC-ABSTRACT:

A composition (I) comprises: (A) an immunogenic agent derived from Helicobacter; and (B) at least one adjuvant chosen from (i) purified saponins from an extract of Quillaja saponaria; (ii) cationic lipids (or their salts) which are weak inhibitors of protein kinase C and have a structure including a lipophilic group derived from cholesterol, a carboxamide or carbamoyl linking group, a spacer arm consisting of a 1-20C alkyl chain and a cationic amine group (primary, secondary, tertiary or quaternary), provided that the lipids are not present in the form of liposomes when (I) contains neither (i) nor (ii); and (iii) glyco-lipo-peptides of formula (II). R1 = 1-50C alkyl (optionally unsaturated); X = -CH2-, -O- or -NH-; R2 = H or as R1; R3-R5 = H or acyl-CO-R6; R6 = 1-10C alkyl; R7 = H, 1-7C alkyl, hydroxymethyl, 1-hydroxyethyl, mercaptomethyl, 2-(methylthio)-ethyl, 3-aminopropyl, 3-ureido-propyl, 3-guanidylpropyl, 4-aminobutyl, carboxymethyl, carbamoylmethyl, 2-carboxyethyl, 2-

carbamoylethyl, benzyl, 4-hydroxybenzyl, 3-indolylmethyl or 4-imidazolylmethyl; R8 =
= H or methyl; R9 = H, acetyl, benzoyl, trichloroacetyl, trifluoroacetyl,
methoxycarbonyl, t-butoxycarbonyl or benzyloxycarbonyl; or R7 + R8 = -(CH₂)₃- .

USE - (I) is useful as a vaccine for the treatment or prevention of Helicobacter infections, e.g. H. pylori infections in humans (associated with gastric and duodenal ulcers, gastritis and gastric carcinoma). (I) induces an immune response of the T-helper 1 type (Th 1) against Helicobacter (claimed).

ADVANTAGE - (I) gives a strong Th 1 response on systemic administration and a degree of protection at least equivalent to that obtained using the mucosal route and a bacterial toxin adjuvant. Specifically the Th 1 immune response measured in the mouse gives IgG2a:IgG1 and IgG2a:IgA ELISA titre ratios of at least 1:100, preferably at least 1:2 (claimed).

ABSTRACTED-PUB-NO: WO 9848836A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/8